Table A.30 Withdrawal due to lack of Arthritis Efficacy (060, 087)

SC-58635 QD VS BID EFFICACY IN KNEE OA
M49-96-02-060

TABLE 21
INCIDENCE OF WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N=231)	SC-58635 200MG QD (N=222)
NUMBER WITHDRAWN DUE TO LACK OF ARTHRITIS EFFICACY	56(24%)	18(8%)	21(9%)

p-VALUES FOR OVERALL COMPARISONS (a): <0.001

p-VALUES FOR TREATMENT COMPARISONS (b):

100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
<0.001	<0.001	0.616

(a) Fisher's Exact test
(b) Pairwise Fisher's Exact test

SC-58635 QD VS BID EFFICACY IN KNEE OA
M49 96 02 087

TABLE 20
INCIDENCE OF WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=243)	SC-58635 100MG BID (N=241)	SC-58635 200MG QD (N=231)
NUMBER WITHDRAWN DUE TO LACK OF ARTHRITIS EFFICACY	55(23%)	27(11%)	24(10%)

p VALUES FOR OVERALL COMPARISONS (a): <0.001

p-VALUES FOR TREATMENT COMPARISONS (b):

100MG BID VS. PLACEBO	200MG QD VS. PLACEBO	200MG QD VS. 100MG BID
<0.001	<0.001	0.662

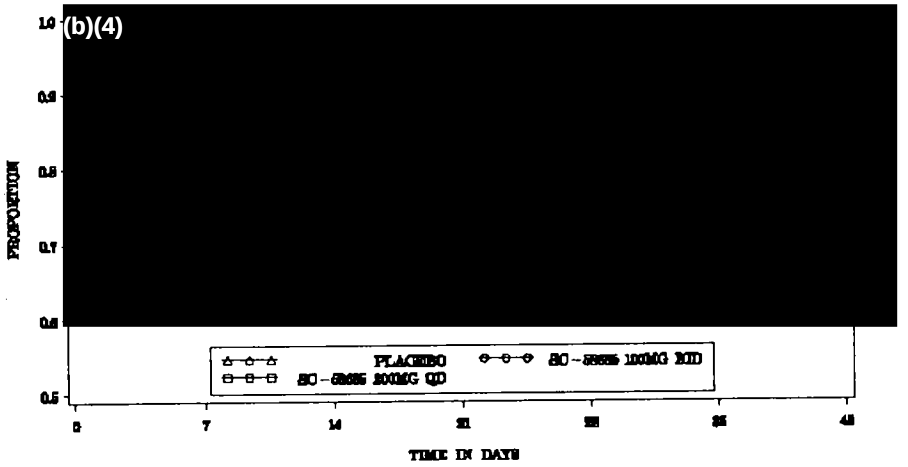
(a) Fisher's Exact test
(b) Pairwise Fisher's Exact test

Table A.31 Time to Withdrawal-Lack of Arthritis Efficacy (060, 087)

SC-58635 QD VS BID EFFICACY IN KNEE OA
M49-98-02-087

TABLE 22
TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
PART 1 OF 2: KAPLAN-MEIER ESTIMATES OF PROPORTION OF PATIENTS
WHO DID NOT WITHDRAW DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)



SC-58635 QD VS BID EFFICACY IN KNEE OA
N49-98-02-087

TABLE 21
TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
PART 1 OF 2: KAPLAN-MEIER ESTIMATES OF PROPORTION OF PATIENTS
WHO DID NOT WITHDRAW DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

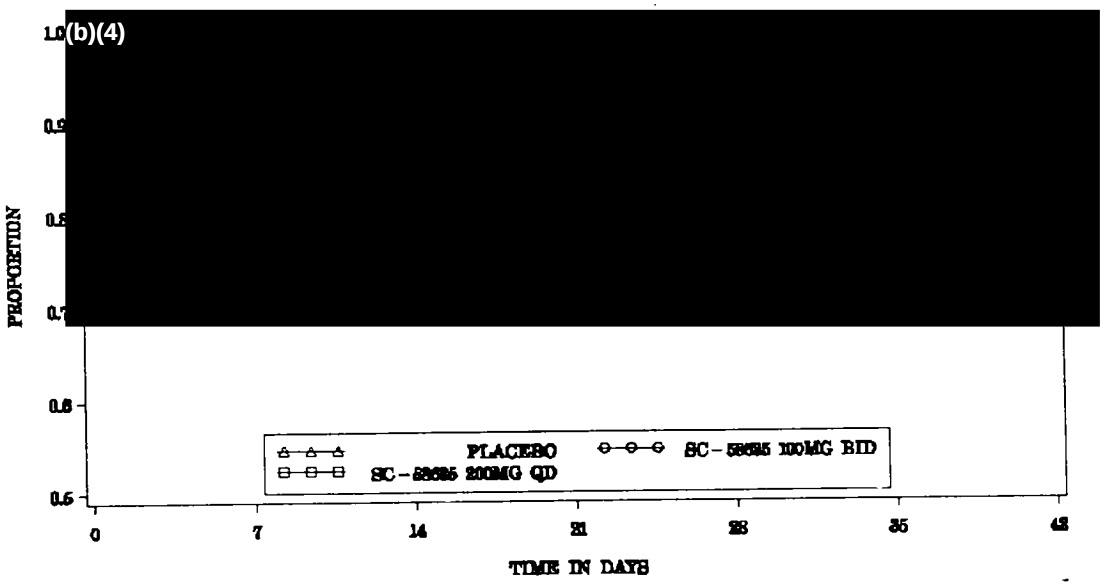


Table A.32 Schedule of Observations and Procedures (protocol 022)

	Screening Visit -7 to -2 day	Baseline Visit (Day 0)	Week 2 (Day 14) (_1 day)	Week 6 (Day 42) (_3 days)	Week 12 (Day 84) (_5 days)	Early Termination
Informed Consent	X					
Medical History	X					
Physical Examination	X				X	X
Clinical laboratory tests (a)	X		X	X (b)	X	X
Discontinue NSAID (c)	X					
Meet Flare Criteria		X				
C-Reactive Protein		X	X	X	X	X
Rheumatoid Factor	X					
SF-36 Health Survey		X			X	X
Health Assessment Questionnaire (HAQ)		X	X	X	X	X
RA Assessments	X (d)	X	X	X	X	X
UGI Endoscopy	X (e)				X	X
Signs and Symptoms		X	X	X	X	X
Dispense Study Medication		X	X	X		
Return and Count Study Medication			X	X	X	X
Dispense Concurrent Meds Diary Card		X	X	X		
Collect Concurrent Meds Diary Card			X	X	X	X

(a) Clinical laboratory tests included **Hematology** (white blood cell [WBC] count with differential, red blood cell [RBC] count, hemoglobin, hematocrit, platelet count [estimate not acceptable], prothrombin time [PT], and partial thromboplastin time [PTT]); **Biochemistry** (sodium, potassium, chloride, calcium, inorganic phosphorus, blood urea nitrogen [BUN], creatinine, total protein, albumin, total bilirubin, uric acid, glucose, alkaline phosphatase, AST [SGOT], ALT [SGPT], creatine kinase [CK]); and **Urinalysis** (pH, specific gravity, WBC, RBC, protein, glucose, ketones, bilirubin). FlexSure® (Baseline) and CLOtest at Final Visit for H. pylori. Serum pregnancy test was performed within seven days before Baseline Arthritis Assessments for women of childbearing potential.

(b) PT and PTT were not performed at the Week 6 Visit.

(c) Patients discontinued oxaprozin and/or piroxicam at least four days before the Baseline Arthritic Assessments.

(d) Screening arthritis assessment data were collected by Searle but not entered into the database.

(e) Pretreatment (Baseline) endoscopy must have been performed within seven days before the first dose of study medication.

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Table A.33 Baseline demographics (study 022, 023-pooled)

Text Table 44. Pooled Baseline Demographic Characteristics and Disease Status for RA Patients By Treatment Group (All Randomized Patients: Pooled Pivotal Studies 022 and 023)

Baseline Characteristic	Number of Patients by Treatment Group				
		Celecoxib			Naproxen
	Placebo (n=452)	100 mg BID (n=468)	200 mg BID (n=454*)	400 mg BID (n=435*)	500 mg BID (n=443)
Age (years)					
Mean (Std. Dev.)	54.2 (12.42)	55.1 (11.99)	54.0 (12.09)	54.0 (12.10)	55.9 (12.09)
Range	(b)(4)				
<65 years - N (%)	350 (77%)	364 (78%)	351 (77%)	344 (79%)	321 (72%)
≥65 years - N (%)	102 (23%)	104 (22%)	103 (23%)	91 (21%)	122 (28%)
Race/Ethnic Origin					
Asian - N (%)	1 (<1%)	4 (<1%)	6 (1%)	4 (<1%)	1 (<1%)
Black - N (%)	36 (8%)	42 (9%)	35 (8%)	35 (8%)	34 (8%)
Caucasian - N (%)	391 (87%)	394 (84%)	380 (84%)	364 (84%)	377 (85%)
Hispanic - N (%)	23 (5%)	25 (5%)	32 (7%)	28 (6%)	28 (6%)
Other - N (%)	1 (<1%)	3 (<1%)	1 (<1%)	4 (<1%)	3 (<1%)
Gender					
Female - N (%)	336 (74%)	346 (74%)	328 (72%)	314 (72%)	313 (71%)
Male - N (%)	116 (26%)	122 (26%)	126 (28%)	121 (28%)	130 (29%)
Disease Duration - Years					
Mean (Std. Dev.)	10.3 (±9.91)	10.7 (±9.01)	10.4 (±9.32)	10.3 (±8.77)	11.0 (±9.80)
Range	0.3-60.0	0.3-53.0	0.3-53.0	0.3-58.0	0.3-55.0
<5 years - N (%)	159 (35%)	135 (29%)	166 (37%)	150 (34%)	143 (32%)
≥5 years - N (%)	293 (65%)	333 (71%)	288 (63%)	285 (66%)	300 (68%)
Corticosteroid Use					
Yes - N (%)	175 (39%)	209 (45%)	172 (38%)	154 (35%)	167 (38%)
No - N (%)	277 (61%)	259 (55%)	282 (62%)	281 (65%)	276 (62%)
Methotrexate Use					
Yes - N (%)	192 (42%)	221 (47%)	205 (45%)	202 (46%)	200 (45%)
No - N (%)	260 (58%)	247 (53%)	249 (55%)	233 (54%)	243 (55%)
Other DMARD Use					
Yes - N (%)	148 (33%)	153 (33%)	139 (31%)	132 (30%)	149 (34%)
No - N (%)	304 (67%)	315 (67%)	315 (69%)	303 (70%)	294 (66%)

Pooled Pivotal Studies 022 and 023)

Baseline Measure	Number of Patients by Treatment Group				
		Celecoxib			Naproxen
	Placebo (n=452)	100 mg BID (n=468)	200 mg BID (n=454*)	400 mg BID (n=435*)	500 mg BID (n=443)
Patient's Global Assessment of Arthritic Condition - N (%)					
Very Good	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Good	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fair	169 (37%)	181 (39%)	184 (41%)	175 (40%)	189 (43%)
Poor	227 (50%)	230 (49%)	212 (47%)	204 (47%)	209 (47%)
Very Poor	56 (12%)	57 (12%)	58 (13%)	56 (13%)	45 (10%)
Number of Tender/Painful Joints					
Mean (Std. Dev.)	28.7 (14.55)	28.2 (14.40)	29.6 (14.99)	28.8 (14.36)	28.2 (14.01)
Range	(b)(4)				
Number of Swollen Joints					
Mean (Std. Dev.)	20.9 (11.83)	20.5 (11.68)	21.7 (12.29)	20.7 (11.80)	20.6 (12.11)
Range	(b)(4)				
Physician's Global Assessment of Arthritic Condition - N (%)					
Very Good	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Good	0 (0%)	1 (<1%)	0 (0%)	0 (0%)	0 (0%)
Fair	199 (44%)	207 (44%)	183 (40%)	182 (42%)	191 (43%)
Poor	220 (49%)	218 (47%)	227 (50%)	216 (50%)	219 (50%)
Very Poor	33 (7%)	42 (9%)	44 (10%)	37 (9%)	32 (7%)

Table A.34.1 Physician's Global Assessment (Protocol 023)

TABLE 20
PHYSICIAN'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 1 OF 4: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	221	228	218	217	218
MEAN	3.6	3.7	3.7	3.7	3.7
STD DEV	0.61	0.65	0.64	0.62	0.63
WEEK 2					
N	221	228	218	217	218
MEAN	3.3	2.9	2.7	2.8	2.7
STD DEV	0.90	0.86	0.84	0.80	0.82
WEEK 6					
N	221	228	218	217	218
MEAN	3.2	2.9	2.8	2.8	2.7
STD DEV	1.01	0.93	0.95	0.91	0.87
WEEK 12					
N	221	228	218	217	218
MEAN	3.3	3.0	2.9	2.8	2.8
STD DEV	1.00	0.95	0.93	0.92	0.92

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor)
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

PHYSICIAN'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 2 OF 4: CATEGORICAL CHANGE ANALYSIS, NUMBER OF PATIENTS (%) (a)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	LINEAR TREND p-VALUE (d)
WEEK 2						<0.001
IMPROVED (b)	22(10%)	44(19%)	60(28%)	46(21%)	55(25%)	
NO CHANGE	187(85%)	179(79%)	151(69%)	171(79%)	161(74%)	
WORSENED (c)	12(5%)	5(2%)	7(3%)	0(0%)	2(<1%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK 6						0.009
IMPROVED (b)	30(14%)	42(18%)	54(25%)	39(18%)	52(24%)	
NO CHANGE	177(80%)	178(78%)	158(72%)	177(82%)	164(75%)	
WORSENED (c)	14(6%)	8(4%)	6(3%)	1(<1%)	2(<1%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK 12						0.001
IMPROVED (b)	27(12%)	42(18%)	48(22%)	44(20%)	55(25%)	
NO CHANGE	178(81%)	179(79%)	164(75%)	171(79%)	160(73%)	
WORSENED (c)	16(7%)	7(3%)	6(3%)	2(<1%)	3(1%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	

p-VALUES FOR TREATMENT COMPARISONS (e) :

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.120	0.423	0.284	<0.001	0.097	0.931	0.273
WEEK 6:	0.001*	0.016*	0.035	0.115	0.753	0.181	<0.001	0.109	0.885	0.156
WEEK 12:	0.003*	0.001*	0.004	0.410	0.681	0.820	<0.001	0.096	0.285	0.229

(a) This table is based on the last observation carried forward approach
(b) Improved is defined as reduction of at least two grades from baseline for grades 3-5 or a change in grade from 2 to 1
(c) Worsened is defined as an increase of at least two grades from baseline for grades 1-3 or a change in grade from 4 to 5
(d) Cochran-Mantel-Haenszel test of linear dose trend stratified by center (Nonzero Correlation), Naproxen group was excluded
(e) Cochran-Mantel-Haenszel test of treatment comparison stratified by center (Row Mean Scores Differ)
* Statistically significant according to the Hochberg procedure (primary pairwise comparisons only)

Table A.34.2 Physician's Global Assessment-continued (Protocol 023)

PHYSICIAN'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 3 OF 4: MEAN CHANGE ANALYSIS (a) (b)
INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.4	-0.8	-1.0	-0.9	-1.0		
STD DEV	0.88	0.92	0.93	0.87	0.90		
LS MEAN CHANGE (c)	-0.3	-0.8	-1.0	-0.9	-1.0		
WEEK 6						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.4	-0.7	-0.9	-0.9	-1.0		
STD DEV	0.96	0.96	1.03	0.89	0.95		
LS MEAN CHANGE (c)	-0.4	-0.7	-0.8	-0.8	-0.9		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.3	-0.7	-0.8	-0.8	-0.9		
STD DEV	0.94	0.97	1.02	0.92	0.98		
LS MEAN CHANGE (c)	-0.3	-0.6	-0.8	-0.8	-0.9		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):

	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	0.78 (0.65 to 0.93)	0.98 (0.83 to 1.15)	0.89 (0.75 to 1.05)
WEEK 6:	0.75 (0.60 to 0.92)	0.89 (0.73 to 1.08)	0.88 (0.73 to 1.07)
WEEK 12:	0.73 (0.58 to 0.92)	0.88 (0.71 to 1.08)	0.91 (0.73 to 1.12)

p-VALUES FOR TREATMENT COMPARISONS (f):

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.009	0.154	0.244	<0.001	0.004	0.790	0.153
WEEK 6:	<0.001*	<0.001*	<0.001	0.113	0.121	0.972	<0.001	0.004	0.205	0.193
WEEK 12:	<0.001*	<0.001*	<0.001	0.135	0.070	0.750	<0.001	0.005	0.199	0.334

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate, the corresponding ROOT MSE are: 0.787 for week 2, 0.868 for week 6, 0.883 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)
* Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

Table A.35.1 Patient's Global Assessment (Protocol 023)

TABLE 17
PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 1 OF 4: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	221	228	218	217	218
MEAN	3.7	3.7	3.7	3.7	3.7
STD DEV	0.68	0.67	0.66	0.64	0.63
WEEK 2					
N	221	228	218	217	218
MEAN	3.4	2.9	2.7	2.7	2.7
STD DEV	0.96	0.90	0.88	0.82	0.83
WEEK 6					
N	221	228	218	217	218
MEAN	3.4	3.0	2.8	2.9	2.8
STD DEV	1.04	0.96	1.00	0.96	0.94
WEEK 12					
N	221	228	218	217	218
MEAN	3.4	3.1	2.9	3.0	2.8
STD DEV	1.05	0.98	0.98	0.92	0.94

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor)
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 2 OF 4: CATEGORICAL CHANGE ANALYSIS, NUMBER OF PATIENTS (%) (a)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	LINEAR TREND p-VALUE (d)
WEEK 2						<0.001
IMPROVED (b)	24(11%)	49(21%)	54(25%)	61(28%)	61(28%)	
NO CHANGE	183(83%)	174(76%)	158(72%)	152(70%)	154(71%)	
WORSENED (c)	14(6%)	5(2%)	6(3%)	4(2%)	3(1%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK 6						0.001
IMPROVED (b)	27(12%)	44(19%)	54(25%)	45(21%)	53(24%)	
NO CHANGE	176(80%)	177(78%)	156(72%)	168(77%)	160(73%)	
WORSENED (c)	18(8%)	7(3%)	8(4%)	4(2%)	5(2%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK 12						0.007
IMPROVED (b)	29(13%)	40(18%)	50(23%)	41(19%)	57(26%)	
NO CHANGE	171(77%)	180(79%)	160(73%)	169(78%)	157(72%)	
WORSENED (c)	21(10%)	8(4%)	8(4%)	7(3%)	4(2%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	

p-VALUES FOR TREATMENT COMPARISONS (e) :

	PRIMARY		SECONDARY						
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.688	0.171	0.335	<0.001	0.099	0.352	0.959
WEEK 6:	0.001*	0.001*	0.004	0.374	0.742	0.618	<0.001	0.217	0.828	0.371
WEEK 12:	0.002*	0.007*	0.016	0.294	0.813	0.411	<0.001	0.026	0.302	0.080

(a) This table is based on the last observation carried forward approach
(b) Improved is defined as reduction of at least two grades from baseline for grades 3-5 or a change in grade from 2 to 1
(c) Worsened is defined as an increase of at least two grades from baseline for grades 1-3 or a change in grade from 4 to 5
(d) Cochran-Mantel-Haenszel test of linear dose trend stratified by center (Monsero Correlation), Naproxen group was excluded
(e) Cochran-Mantel-Haenszel test of treatment comparison stratified by center (Row Mean Scores Differ)
* Statistically significant according to the Hochberg procedure (primary pairwise comparisons only)

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Table A.35.2 Patient's Global Assessment-continued (Protocol 023)

TABLE 17
PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS
PART 3 OF 4: MEAN CHANGE ANALYSIS (a) (b)
INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.4	-0.8	-1.0	-1.0	-1.0		
STD DEV	0.93	0.99	0.90	0.90	0.91		
LS MEAN CHANGE (c)	-0.3	-0.8	-1.0	-1.0	-1.0		
WEEK 6						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.4	-0.7	-0.8	-0.8	-0.9		
STD DEV	0.96	0.99	1.04	0.95	0.99		
LS MEAN CHANGE (c)	-0.3	-0.7	-0.8	-0.8	-0.9		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.3	-0.6	-0.8	-0.7	-0.9		
STD DEV	0.97	0.97	1.01	0.96	1.00		
LS MEAN CHANGE (c)	-0.3	-0.6	-0.8	-0.7	-0.9		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	0.78 (0.64 to 0.93)	0.95 (0.81 to 1.12)	0.94 (0.80 to 1.11)
WEEK 6:	0.75 (0.59 to 0.94)	0.92 (0.74 to 1.13)	0.88 (0.70 to 1.08)
WEEK 12:	0.66 (0.50 to 0.86)	0.89 (0.71 to 1.12)	0.82 (0.65 to 1.04)

p-VALUES FOR TREATMENT COMPARISONS (f):

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.024	0.032	0.913	<0.001	0.004	0.548	0.478
WEEK 6:	<0.001*	<0.001*	<0.001	0.081	0.197	0.656	<0.001	0.010	0.405	0.201
WEEK 12:	<0.001*	<0.001*	0.001	0.024	0.122	0.479	<0.001	<0.001	0.304	0.083

(a) This table is based on the last obeservation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate, the corresponding ROOT MSE are: 0.826 for week 2, 0.914 for week 6, 0.909 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)
* Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

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Table A.36.1 Number of Tender/Painful Joints (Protocol 022)

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TABLE 30
NUMBER OF TENDER/PAINFUL JOINTS
PART 1 OF 5: OBSERVED MEANS (a) (b)

INTENT TO TREAT COHORT (ITT)

	PLACEBO (N 231)	SC-58635 100MG BID (N=240)	SC-58635 200MG BID (N 235)	SC-58635 400MG BID (N 217)	NAPROXEN 500MG BID (N 225)
BASELINE					
N	231	240	235	217	225
MEAN	29.7	29.6	31.0	28.2	28.7
STD DEV	14.84	14.94	15.24	14.31	14.27
WEEK 2					
N	231	240	235	217	225
MEAN	21.5	19.5	18.8	18.9	18.0
STD DEV	15.43	15.29	15.77	14.38	15.20
WEEK 6					
N	231	240	235	217	225
MEAN	20.8	18.5	18.7	16.5	18.2
STD DEV	16.65	16.39	15.71	14.99	15.75
WEEK 12					
N	231	240	235	217	225
MEAN	21.1	17.9	18.6	16.5	18.6
STD DEV	17.27	16.84	16.24	14.98	16.06

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 44 with lower score as better

NUMBER OF TENDER/PAINFUL JOINTS
PART 2 OF 5: PATIENT'S OVERALL STATUS BY CHANGE FROM BASELINE, NUMBER OF PATIENTS (%) (a)

INTENT TO TREAT COHORT (ITT)

	PLACEBO (N 231)	SC-58635 100MG BID (N 240)	SC-58635 200MG BID (N 235)	SC-58635 400MG BID (N 217)	NAPROXEN 500MG BID (N 225)	LINEAR TREND p-VALUE (d)
WEEK 2						0.001
IMPROVED (b)	72(31%)	104(43%)	112(48%)	103(47%)	105(47%)	
NO CHANGE	148(64%)	129(54%)	116(49%)	108(50%)	112(50%)	
WORSENED (c)	11(5%)	7(3%)	7(3%)	6(3%)	8(4%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	
WEEK 6						0.004
IMPROVED (b)	89(39%)	116(49%)	108(46%)	109(50%)	108(48%)	
NO CHANGE	126(55%)	107(45%)	122(52%)	104(48%)	105(47%)	
WORSENED (c)	16(7%)	15(6%)	5(2%)	4(2%)	12(5%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	
WEEK 12						0.014
IMPROVED (b)	95(41%)	127(53%)	115(49%)	104(48%)	98(44%)	
NO CHANGE	120(52%)	96(40%)	111(47%)	105(48%)	112(50%)	
WORSENED (c)	16(7%)	17(7%)	9(3%)	8(4%)	15(7%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	

(a) VALUES ARE OBSERVED COMPARISONS

	PRIMARY			SECONDARY					
	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2	0.002*	0.000*	0.002	0.324	0.277	0.945	0.001	0.549	0.662	0.732
WEEK 6	0.004*	0.000*	0.017*	0.064	0.497	0.414	0.031	0.788	0.960	0.656
WEEK 12	0.030*	0.015*	0.062	0.781	0.781	0.754	0.225	0.091	0.199	0.264

(a) This table is based on the last observation carried forward approach
(b) Response is defined as number of improved joints minus number of worsened joints is larger than or equal to 50% of the number of joints with baseline score > 0
(c) Worsened is defined as number of worsened joints minus number of improved joints is larger than or equal to 50% of the number of joints with baseline score > 0
(d) Cochran-Mantel-Haenszel test of linear dose trend stratified by center. Nonzero correlation. Naproxen group was excluded
(e) Cochran Mantel Haenszel test of treatment comparison stratified by center. Row Mean Scores Differ
* statistically significant at the [illegible] level [illegible]

BEST POSSIBLE

Table A.36.2 Number of Tender/Painful Joints-(Protocol 022)

PART 1 OF 2. MEAN CHANGE ANALYSIS (a) (b)
INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=211)	SC-58635 100MG BID (N=240)	SC-58635 200MG BID (N=235)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=225)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
						<0.001	<0.001
WEEK 2							
OBSERVED MEAN CHANGE	-7.6	-11.1	-12.2	-11.3	-10.2		
STD DEV	13.51	13.73	12.77	13.68	13.67		
LS MEAN CHANGE (c)	-7.5	-11.2	-12.0	-11.6	-10.3		
WEEK 6						0.004	<0.001
OBSERVED MEAN CHANGE	-9.9	-13.1	-13.3	-13.7	-12.1		
STD DEV	14.75	14.36	13.67	13.63	14.53		
LS MEAN CHANGE (c)	-9.8	-13.3	-13.9	-13.8	-12.3		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-9.6	-13.8	-12.6	-13.7	-12.8		
STD DEV	14.27	14.14	13.99	13.59	13.16		
LS MEAN CHANGE (c)	-9.3	-12.9	-12.3	-13.4	-12.1		

Q RATIO WITH 95% CONFIDENCE INTERVALS (e): 100MG BID VS. NAPROXEN 200MG BID VS. NAPROXEN 400MG BID VS. NAPROXEN

WEEK 2:	1.05 (0.87 to 1.27)	1.11 (0.92 to 1.34)	1.11 (0.92 to 1.34)
WEEK 6:	1.07 (0.87 to 1.33)	1.13 (0.92 to 1.40)	1.16 (0.94 to 1.43)
WEEK 12:	1.19 (0.96 to 1.49)	1.22 (0.98 to 1.52)	1.23 (0.99 to 1.54)

p-VALUES FOR TREATMENT COMPARISONS (f):

	PRIMARY: 200MG BID VS. PLACEBO	PRIMARY: 400MG BID VS. PLACEBO	PRIMARY: 500MG BID VS. PLACEBO	SECONDARY: 200MG BID VS. 100MG BID	SECONDARY: 400MG BID VS. 100MG BID	SECONDARY: 400MG BID VS. 200MG BID	SECONDARY: NAPROXEN VS. PLACEBO	SECONDARY: NAPROXEN VS. 100MG BID	SECONDARY: NAPROXEN VS. 200MG BID	SECONDARY: NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.111	0.535	0.582	0.001	0.607	0.247	0.266
WEEK 6:	0.001*	<0.001*	0.001	0.071	0.450	0.608	0.045	0.483	0.222	0.199
WEEK 12:	<0.001*	<0.001*	0.001	0.410	0.736	0.936	0.133	0.184	0.065	0.055

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 48 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate, the corresponding ROOT MSE are: 11.005 for week 2, 12.177 for week 6, 12.595 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is obtained as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)
* Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

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Table A.37.1 Number of Swollen Joints (Protocol 023)

TABLE 19
NUMBER OF SWOLLEN JOINTS
PART 1 OF 5: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	221	228	218	217	218
MEAN	19.7	20.0	21.2	20.5	20.6
STD DEV	11.95	11.77	11.69	10.93	12.00
WEEK 2					
N	221	228	218	217	218
MEAN	16.0	13.7	13.6	13.7	13.4
STD DEV	12.73	10.78	11.10	9.18	10.22
WEEK 6					
N	221	228	218	217	218
MEAN	15.8	13.8	14.2	13.5	13.6
STD DEV	13.43	10.87	12.21	9.59	11.32
WEEK 12					
N	221	228	218	217	218
MEAN	16.0	13.9	14.4	13.6	13.9
STD DEV	13.39	10.81	12.26	9.47	11.76

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 66 with lower score as better
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

NUMBER OF SWOLLEN JOINTS
PART 2 OF 5: PATIENT'S OVERALL STATUS IN CHANGE FROM BASELINE, NUMBER OF PATIENTS (%) (a)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	LINEAR TREND p-VALUE (d)
						0.191
WEEK 2						
IMPROVED (b)	66(30%)	72(32%)	89(41%)	68(31%)	86(39%)	
NO CHANGE	136(62%)	147(64%)	120(55%)	142(65%)	127(58%)	
WORSENED (c)	19(9%)	9(4%)	9(4%)	7(3%)	5(2%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
						0.324
WEEK 6						
IMPROVED (b)	81(37%)	76(33%)	90(41%)	76(35%)	93(43%)	
NO CHANGE	117(53%)	144(63%)	121(56%)	132(61%)	117(54%)	
WORSENED (c)	23(10%)	8(4%)	7(3%)	9(4%)	8(4%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
						0.069
WEEK 12						
IMPROVED (b)	67(30%)	73(32%)	90(41%)	74(34%)	92(42%)	
NO CHANGE	133(60%)	145(64%)	119(55%)	134(62%)	113(52%)	
WORSENED (c)	21(10%)	10(4%)	9(4%)	9(4%)	13(6%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	

p-VALUES FOR TREATMENT COMPARISONS (e) :

	PRIMARY: 200MG BID VS. PLACEBO	PRIMARY: 400MG BID VS. PLACEBO	SECONDARY: 100MG BID VS. PLACEBO	SECONDARY: 200MG BID VS. 100MG BID	SECONDARY: 400MG BID VS. 100MG BID	SECONDARY: 400MG BID VS. 200MG BID	SECONDARY: NAPROXEN VS. PLACEBO	SECONDARY: NAPROXEN VS. 100MG BID	SECONDARY: NAPROXEN VS. 200MG BID	SECONDARY: NAPROXEN VS. 400MG BID
WEEK 2:	0.003*	0.468	0.365	0.054	0.879	0.022	0.010	0.095	0.764	0.065
WEEK 6:	0.033	0.896	0.931	0.033	0.653	0.101	0.051	0.047	0.902	0.081
WEEK 12:	0.002*	0.269	0.524	0.024	0.701	0.083	0.007	0.074	0.669	0.148

(a) This table is based on the last observation carried forward approach
(b) Improved is defined as number of improved joints minus number of worsened joints is larger than or equal to 50% of the number of joints with baseline score > 0
(c) Worsened is defined as number of worsened joints minus number of improved joints is larger than or equal to 50% of the number of joints with baseline score > 0
(d) Cochran-Mantel-Haenszel test of linear dose trend stratified by center (Nonzero Correlation), Naproxen group was excluded
(e) Cochran-Mantel-Haenszel test of treatment comparison stratified by center (Row Mean Scores Differ)
* Statistically significant according to the Hochberg procedure (primary pairwise comparisons only)

Table A.37.2 Number of Swollen Joints (Protocol 023)

NUMBER OF SWOLLEN JOINTS
PART 3 OF 5: MEAN CHANGE ANALYSIS (a) (b)
INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-3.8	-6.3	-7.6	-6.8	-7.2		
STD DEV	9.23	8.32	9.57	8.18	9.08		
LS MEAN CHANGE (c)	-3.9	-6.3	-7.1	-6.6	-6.8		
WEEK 6						0.003	0.001
OBSERVED MEAN CHANGE	-3.9	-6.2	-7.0	-6.9	-7.0		
STD DEV	10.01	9.46	9.42	8.98	8.99		
LS MEAN CHANGE (c)	-3.8	-5.9	-6.2	-6.4	-6.4		
WEEK 12						0.006	0.002
OBSERVED MEAN CHANGE	-3.7	-6.0	-6.8	-6.9	-6.6		
STD DEV	10.40	9.61	9.70	9.67	10.05		
LS MEAN CHANGE (c)	-3.7	-5.9	-6.0	-6.4	-6.1		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):

	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	0.92 (0.74 to 1.15)	1.04 (0.85 to 1.29)	0.96 (0.77 to 1.20)
WEEK 6:	0.93 (0.71 to 1.20)	0.97 (0.75 to 1.25)	1.00 (0.77 to 1.29)
WEEK 12:	0.97 (0.73 to 1.28)	0.99 (0.75 to 1.31)	1.04 (0.79 to 1.37)

p-VALUES FOR TREATMENT COMPARISONS (f):

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.244	0.698	0.443	<0.001	0.453	0.681	0.721
WEEK 6:	0.002*	0.001*	0.006	0.725	0.563	0.822	<0.001	0.546	0.803	0.981
WEEK 12:	0.004*	0.001*	0.006	0.866	0.582	0.706	0.003	0.818	0.952	0.751

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 66 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate, the corresponding ROOT MSE are: 7.375 for week 2, 8.151 for week 6, 8.456 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)
* Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

Table A.38.1 ACR-20 Responder Index (Protocol 023-ITT)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA
M49-96-02-023

TABLE 16
CATEGORIAL STATUS BASED ON THE ACR RESPONDERS INDEX (20%) (a)
NUMBER OF PATIENTS (%)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	LINEAR TREND P-VALUE (c)
WEEK2						<0.001
IMPROVED (b)	55(25%)	95(42%)	101(46%)	93(43%)	97(44%)	
NOT IMPROVED	166(75%)	133(58%)	117(54%)	124(57%)	121(56%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK6						<0.001
IMPROVED (b)	60(27%)	87(38%)	89(41%)	94(43%)	101(46%)	
NOT IMPROVED	161(73%)	141(62%)	129(59%)	123(57%)	117(54%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	
WEEK12						<0.001
IMPROVED (b)	50(23%)	68(30%)	86(39%)	79(36%)	91(42%)	
NOT IMPROVED	171(77%)	160(70%)	132(61%)	138(64%)	127(58%)	
TOTAL	221(100%)	228(100%)	218(100%)	217(100%)	218(100%)	

P-VALUE FOR TREATMENT COMPARISONS (d):

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK2 :	<0.001*	<0.001*	<0.001	0.261	0.835	0.348	<0.001	0.537	0.698	0.507
WEEK6 :	0.002*	<0.001*	0.015	0.507	0.299	0.661	<0.001	0.096	0.294	0.507
WEEK12 :	<0.001*	0.002*	0.060	0.038	0.198	0.432	<0.001	0.011	0.585	0.242

Note: The ITT cohort includes only patients who had at least one dose of study medication
(a) This table is based on the last observation carried forward approach
(b) Improved: At least 20% improvement from baseline in the number of tender/painful joints and in the number of swollen joints as well as at least 20% improvement from baseline in at least three of the following assessments: 1) Physician's Global 2) Patient's Global 3) Patient's Assessment of Pain 4) C-Reactive Protein 5) HAQ Functional Disability Index
(c) Cochran-Mantel-Haenszel test of linear dose trend stratified by center, p-value for Nonzero Correlation, naproxen was excluded
(d) Cochran-Mantel-Haenszel test of treatment comparison stratified by center, p-value for Row Mean Scores Differ
* Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

BEST POSSIBLE

Table A.38.2 ACR-20 Responder Index (Protocol 022, ITT)

SC-58635 COMPARATIVE EFFICACY AND UGI SAFETY VS NAPROXEN IN RA
N49-96-02-022

TABLE 18
CATEGORICAL STATUS BASED ON THE ACR RESPONDERS INDEX (20%) (a)
NUMBER OF PATIENTS (%)

INTENT TO TREAT COHORT (ITT)

	PLACEBO (N=231)	SC-58635 100MG BID (N=240)	SC-58635 200MG BID (N=235)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=225)	LINEAR TREND P-VALUE (c)
WEEK2						<0.001
IMPROVED (b)	51(22%)	95(40%)	115(49%)	89(41%)	69(31%)	
NOT IMPROVED	180(78%)	145(60%)	120(51%)	128(59%)	156(69%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	
WEEK6						<0.001
IMPROVED (b)	64(28%)	93(39%)	114(49%)	87(40%)	84(37%)	
NOT IMPROVED	167(72%)	147(61%)	121(51%)	130(60%)	141(63%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	
WEEK12						0.005
IMPROVED (b)	66(29%)	95(40%)	103(44%)	85(39%)	81(36%)	
NOT IMPROVED	165(71%)	145(60%)	132(56%)	132(61%)	144(64%)	
TOTAL	231(100%)	240(100%)	235(100%)	217(100%)	225(100%)	

P-VALUE FOR TREATMENT COMPARISONS (d):

	PRIMARY		SECONDARY							
	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK2 :	<0.001*	<0.001*	<0.001	0.060	0.586	0.160	<0.001	0.868	0.028	0.561
WEEK6 :	<0.001*	0.035*	0.008	0.035	0.693	0.047	0.016	0.817	0.011	0.578
WEEK12 :	<0.001*	0.012*	0.005	0.270	0.956	0.320	0.049	0.445	0.077	0.562

(a) This table is based on the last observation carried forward approach
(b) Improved: At least 20% improvement from baseline in the number of tender/painful joints and in the number of swollen joints as well as at least 20% improvement from baseline in at least three of the following assessments: 1) Physician's Global 2) Patient's Global 3) Patient's Assessment of Pain 4) C-Reactive Protein 5) HAQ Functional Disability Index
(c) Cochran-Mantel-Haenszel test of linear dose trend stratified by center, p-value for Nonzero Correlation, naproxen was excluded
(d) Cochran-Mantel-Haenszel test of treatment comparison stratified by center, p-value for Row Mean Scores Differ
* Statistically significant according to the Hochberg procedure (primary pairwise comparisons only)

BEST POSSIBLE

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Table A.38.3 ACR-20 Responder Index (Protocol 023-Evaluable)

APPENDIX A.2.1
CATEGORICAL STATUS BASED ON THE ACR RESPONDERS INDEX (20%)
NUMBER OF PATIENTS (%)

EVALUABLE COHORT

	PLACEBO* (N 223)*	DC-19936 100MG BID (N 222)*	DC-19936 200MG BID (N 219)*	DC-19936 400MG BID (N 227)*	NAPROXEN 500MG BID (N 216)*	P-VALUE (a) (b)
WEEK 4						0.036
IMPROVED (a)	67(30%)	85(45%)	94(47%)	82(45%)	92(51%)	
NOT IMPROVED	99(70%)	97(54%)	94(53%)	93(55%)	87(49%)	
TOTAL	166(100%)	182(100%)	178(100%)	175(100%)	179(100%)	
WEEK 6						0.080
IMPROVED (a)	89(51%)	92(54%)	68(52%)	78(61%)	85(60%)	
NOT IMPROVED	36(49%)	96(46%)	64(48%)	50(39%)	56(40%)	
TOTAL	76(100%)	211(100%)	132(100%)	128(100%)	141(100%)	
WEEK 12						0.022
IMPROVED (a)	27(46%)	46(54%)	64(60%)	65(60%)	62(62%)	
NOT IMPROVED	31(54%)	39(51%)	38(37%)	43(40%)	41(37%)	
TOTAL	58(100%)	85(100%)	102(100%)	108(100%)	103(100%)	
FINAL						0.001
IMPROVED (a)	40(24%)	77(44%)	93(49%)	89(49%)	93(53%	
NOT IMPROVED	94(57%)	100(56%)	104(54%)	97(52%)	96(51%	
TOTAL	134(100%)	177(100%)	197(100%)	186(100%)	189(100%	

P-VALUE FOR TREATMENT COMPARISONS (c):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 4 :	0.018	0.021	0.018	0.969	0.850	0.906	<0.001	0.338	0.273	0.354
WEEK 6 :	0.611	0.589	0.175	0.819	0.139	0.155	0.046	0.295	0.265	0.710
WEEK 12:	0.442	0.139	0.229	0.033	0.069	0.528	0.009	0.014	0.980	0.664
FINAL :	0.108	0.037	0.018	0.176	0.048	0.642	0.004	0.037	0.369	0.983

(a) Improved: At least 20% improvement from baseline in the number of tender/painful joints and in the number of swollen joints as well as at least 20% improvement from baseline in at least three of the following assessments: 1) Physician's Global 2) Patient's Global 3) Patient's Assessment of Pain 4) C-Reactive Protein 5) HAQ Functional Disability Index

(b) Cochran Mantel Haenszel test of linear dose trend stratified by center, p-value for Nonzero Correlation, naproxen was excluded

(c) Cochran-Mantel-Haenszel test of treatment comparisons stratified by center, p-value for Row Mean Scores Differ

* All randomized patients

Table A.39.1 ACR-50 Responder Index (Protocol 022-ITT)

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Table A.39.2 ACR-50 Responder Index (Protocol 023-ITT)

SC-58125 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA
M69 96 02 023

TABLE 14
CATEGORICAL STATUS BASED ON THE ACR IMPROVEMENT INDEX (ACR50) (a)
NUMBER OF PATIENTS (%)

INTENT TO TREAT (WORST CASE)

	PLACEBO	SC-58125 100MG BID	SC-58125 200MG BID	SC-58125 400MG BID	NAPROXEN 500MG BID	LINEAR TREND P VALUE (c)
	(N 221)	(N 228)	(N 218)	(N 227)	(N 219)	
WEEK2						0.060
IMPROVED (b)	12(5%)	26(11%)	37(17%)	27(12%)	23(10%)	
NOT IMPROVED	209(95%)	202(89%)	181(83%)	200(88%)	196(90%)	
TOTAL	221(100%)	228(100%)	218(100%)	227(100%)	219(100%)	
WEEK6						0.009
IMPROVED (b)	15(7%)	22(10%)	35(16%)	25(11%)	32(15%)	
NOT IMPROVED	206(93%)	206(90%)	183(84%)	202(89%)	186(85%)	
TOTAL	221(100%)	228(100%)	218(100%)	227(100%)	218(100%)	
WEEK12						0.007
IMPROVED (b)	13(6%)	23(10%)	38(17%)	27(12%)	39(18%)	
NOT IMPROVED	208(94%)	205(90%)	180(83%)	200(88%)	179(82%)	
TOTAL	221(100%)	228(100%)	218(100%)	227(100%)	218(100%)	

P-VALUE FOR TREATMENT COMPARISONS (d):

	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK2	<0.001	0.010	0.019	0.115	0.795	0.142	<0.001	0.275	0.453	0.329
WEEK6	0.001	0.044	0.045	0.042	0.598	0.157	0.006	0.218	0.052	[illegible]
WEEK12	<0.001	0.017	0.081	0.033	0.519	0.112	<0.001	0.024	0.610	0.129

Note: The ITT cohort includes only patients who had at least one dose of study medication

(a) This table is based on the last observation carried forward approach

(b) Improved: At least 20% improvement from baseline in the number of tender/painful joints and in the number of swollen joints as well as at least 50% improvement from baseline in at least three of the following assessments: 1) Physician's Global 2) Patient's Global 3) Patient's Assessment of Pain 4) C-Reactive Protein 5) HAQ Functional Disability Index

(c) Cochran-Mantel-Haenszel test of linear dose trend stratified by center, prvalue for Nonzero Correlation, naproxen was excluded

(d) Cochran-Mantel-Haenszel test of "treatment comparison stratified by center, prvalue for Row Mean Scores Differ

BEST POSSIBLE

APPEARS THIS WAY ON ORIGINAL

Table A.40 Patient's Assessment of Arthritis Pain-VAS (Protocol 023)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA
M49-96-02-023

TABLE 21
PATIENT'S ASSESSMENT OF ARTHRITIS PAIN (VAS)
PART 1 OF 3: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	220	228	218	216	218
MEAN	68.1	66.1	67.9	67.8	66.8
STD DEV	19.57	20.13	19.90	19.70	18.48
WEEK 2					
N	220	228	218	217	218
MEAN	58.7	45.8	41.4	42.2	40.6
STD DEV	27.15	26.25	25.10	24.62	24.36
WEEK 6					
N	221	228	218	217	218
MEAN	60.5	47.8	46.5	45.6	43.7
STD DEV	27.86	27.74	28.38	26.39	25.77
WEEK 12					
N	221	228	218	217	218
MEAN	62.0	51.0	47.0	48.7	44.6
STD DEV	27.88	28.41	29.03	26.48	27.43

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 mm with lower score as better
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

PATIENT'S ASSESSMENT OF ARTHRITIS PAIN (VAS)
PART 2 OF 3: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-9.4	-20.3	-26.5	-25.6	-26.2		
STD DEV	25.81	24.27	24.12	23.61	25.02		
LS MEAN CHANGE (e)	-8.8	-20.7	-26.0	-25.1	-26.1		
WEEK 6						<0.001	<0.001
OBSERVED MEAN CHANGE	-7.4	-18.3	-21.4	-22.2	-23.1		
STD DEV	25.59	25.94	28.80	27.60	26.35		
LS MEAN CHANGE (e)	-6.1	-18.3	-20.4	-21.1	-22.5		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-6.1	-15.1	-20.9	-19.0	-22.1		
STD DEV	25.07	26.83	29.12	27.10	27.77		
LS MEAN CHANGE (e)	-5.5	-15.5	-20.4	-18.5	-22.0		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	0.79 (0.65 to 0.96)	1.00 (0.84 to 1.18)	0.96 (0.80 to 1.14)
WEEK 6:	0.81 (0.63 to 1.03)	0.90 (0.72 to 1.14)	0.94 (0.75 to 1.17)
WEEK 12:	0.71 (0.53 to 0.92)	0.93 (0.73 to 1.18)	0.84 (0.65 to 1.07)

p-VALUES FOR TREATMENT COMPARISONS (f):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.014	0.046	0.655	<0.001	0.012	0.962	0.620
WEEK 6:	<0.001	<0.001	<0.001	0.380	0.233	0.753	<0.001	0.073	0.364	0.555
WEEK 12:	<0.001	<0.001	<0.001	0.042	0.226	0.418	<0.001	0.007	0.519	0.146

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 (mm) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate, the corresponding ROOT MSE are: 22.76 for week 2, 24.84 for week 6, and 25.35 for week 12
(d) From a contrast statement from analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)

Table A.41 C-Reactive Protein (Protocol 023)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA
M49-96-02-023

TABLE 26.1
C-REACTIVE PROTEIN
PART 1 OF 2: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	215	222	214	210	210
MEAN	15572.1	16464.0	17887.9	15590.5	15481.0
STD DEV	15608.32	19890.11	20419.69	15790.92	18677.37
WEEK 2					
N	220	228	218	216	217
MEAN	15154.5	16592.1	17367.0	16935.2	14023.0
STD DEV	16015.79	20979.44	20191.55	17566.50	14229.42
WEEK 6					
N	221	228	218	217	218
MEAN	16470.6	17693.0	17243.1	18838.7	14504.6
STD DEV	18308.60	22025.47	19269.39	20799.01	15386.34
WEEK 12					
N	221	228	218	217	218
MEAN	18040.7	16877.2	16825.7	17963.1	13756.9
STD DEV	27587.43	20610.35	18969.70	19711.54	13783.06

(a) This table is based on the last observation carried forward approach
(b) Unit of measurement : ug/L
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

C-REACTIVE PROTEIN
PART 2 OF 2: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						0.168	0.159
OBSERVED MEAN CHANGE	-325.6	333.3	-359.8	1409.5	-1352.4		
STD DEV	12853.82	11978.74	15069.37	12330.92	12025.87		
LS MEAN CHANGE (c)	-300.7	703.6	374.8	1535.4	-1247.1		
WEEK 6						0.016	0.172
OBSERVED MEAN CHANGE	1004.7	1369.4	-542.1	1347.6	-823.8		
STD DEV	15781.95	13404.89	12134.44	15726.68	13705.46		
LS MEAN CHANGE (c)	1420.0	2106.5	395.5	3871.3	-340.8		
WEEK 12						0.040	0.912
OBSERVED MEAN CHANGE	2604.7	536.0	-967.3	2595.2	-1600.0		
STD DEV	26246.44	14431.49	14446.40	16625.43	12311.82		
LS MEAN CHANGE (c)	2778.4	1236.1	37.6	2990.0	-1269.8		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	-0.56 (NON-ESTIMABLE)	-0.30 (NON-ESTIMABLE)	-1.23 (NON-ESTIMABLE)
WEEK 6:	-6.18 (NON-ESTIMABLE)	-1.16 (NON-ESTIMABLE)	-11.4 (NON-ESTIMABLE)
WEEK 12:	-0.97 (NON-ESTIMABLE)	-0.03 (NON-ESTIMABLE)	-2.35 (NON-ESTIMABLE)

p-VALUES FOR TREATMENT COMPARISONS (f):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	0.383	0.561	0.115	0.775	0.472	0.320	0.417	0.091	0.164	0.018
WEEK 6:	0.595	0.432	0.061	0.186	0.175	0.008	0.179	0.060	0.574	0.001
WEEK 12:	0.333	0.088	0.896	0.452	0.273	0.068	0.012	0.117	0.418	0.009

(a) This table is based on the last observation carried forward approach
(b) Unit of measurement : ug/L with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate, the corresponding ROOT MSE are: 11963 for week 2, 13440 for week 6, and 16562 for week 12
(d) From a contrast statement from analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)

Table A.42 HAQ Functional Disability Index (Protocol 023)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA
E49-96-02-023

TABLE 25
HAQ FUNCTIONAL DISABILITY INDEX
PART 1 OF 3: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE					
N	219	226	217	216	218
MEAN	1.4	1.4	1.3	1.3	1.4
STD DEV	0.68	0.70	0.67	0.63	0.68
WEEK 2					
N	221	228	218	217	218
MEAN	1.3	1.1	1.0	1.0	1.1
STD DEV	0.67	0.69	0.68	0.64	0.67
WEEK 6					
N	221	228	218	217	218
MEAN	1.3	1.2	1.1	1.0	1.1
STD DEV	0.72	0.71	0.72	0.66	0.69
WEEK 12					
N	221	228	218	217	218
MEAN	1.3	1.3	1.1	1.1	1.1
STD DEV	0.73	0.70	0.73	0.67	0.68

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 3 with lower score as less disability
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

HAQ FUNCTIONAL DISABILITY INDEX
PART 2 OF 3: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL p-VALUE(c)	LINEAR TREND p-VALUE(d)
WEEK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.1	-0.2	-0.3	-0.3	-0.3		
STD DEV	0.44	0.42	0.45	0.47	0.47		
LS MEAN CHANGE (c)	-0.1	-0.2	-0.3	-0.3	-0.3		
WEEK 6						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.1	-0.2	-0.3	-0.3	-0.3		
STD DEV	0.49	0.43	0.51	0.52	0.48		
LS MEAN CHANGE (c)	-0.1	-0.2	-0.3	-0.3	-0.3		
WEEK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.1	-0.1	-0.2	-0.2	-0.3		
STD DEV	0.49	0.44	0.51	0.53	0.48		
LS MEAN CHANGE (c)	-0.1	-0.1	-0.2	-0.2	-0.3		

Q-RATIO WITH 95% CONFIDENCE INTERVALS (e):	100MG BID VS. NAPROXEN	200MG BID VS. NAPROXEN	400MG BID VS. NAPROXEN
WEEK 2:	0.83 (0.59 to 1.15)	1.08 (0.82 to 1.45)	1.05 (0.79 to 1.42)
WEEK 6:	0.69 (0.43 to 1.04)	1.07 (0.76 to 1.51)	0.99 (0.69 to 1.41)
WEEK 12:	0.56 (0.30 to 0.90)	0.94 (0.64 to 1.38)	0.98 (0.67 to 1.43)

p-VALUES FOR TREATMENT COMPARISONS (f):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.080	0.124	0.837	<0.001	0.244	0.560	0.707
WEEK 6:	0.006	<0.001	<0.001	0.025	0.074	0.658	<0.001	0.065	0.698	0.956
WEEK 12:	0.103	<0.001	<0.001	0.031	0.017	0.813	<0.001	0.012	0.738	0.923

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 3 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate, the corresponding ROOT MSE are: 0.424 for week 2, 0.458 for week 6, and 0.462 for week 12
(d) From a contrast statement from analysis of Covariance model in (c), Naproxen group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxen group
(f) From a contrast statement from Analysis of Covariance model in (c)

Table A.43 Withdrawal-Lack of Arthritis Efficacy (Protocols 022, 023)

Text Table 40. Reasons for Study Termination (All Randomized Patients: 12-Week Pivotal Studies 022 and 023 and 12-Week Pooled Pivotal Studies)

	Number of Rheumatoid Arthritis Patients by Treatment Group				
		Celecoxib			Naproxen
Study	Placebo	100 mg BID	200 mg BID	400 mg BID	500 mg BID
Study 022	**(n=231)**	**(n=240)**	**(n=235)**	**(n=218)[a]**	**(n=225)**
Total Completed	**101 (44%)**	**154 (64%)**	**158 (67%)**	**137 (63%)**	**138 (61%)**
Total Withdrawn	**130 (56%)**	**86 (36%)**	**77 (33%)**	**81 (37%)**	**87 (39%)**
Lost to Follow-up	3 (1%)	1 (<1%)	3 (1%)	1 (<1%)	1 (<1%)
Pre-Existing Violation	2 (<1%)	1 (<1%)	3 (1%)	2 (<1%)	0 (0%)
Protocol Non-Compliance	10 (4%)	4 (2%)	4 (2%)	7 (3%)	9 (4%)
Treatment Failure	104 (45%)	67 (28%)	50 (21%)	59 (27%)	65 (29%)
Adverse Event	11 (5%)	13 (5%)	17 (7%)	12 (6%)	12 (5%)
Study 023	**(n=221)**	**(n=228)**	**(n=219)[a]**	**(n=217)**	**(n=218)**
Total Completed	**78(35%)**	**117 (51%)**	**124 (57%)**	**126 (58%)**	**133(61%)**
Total Withdrawn	**143 (65%)**	**111 (49%)**	**95 (43%)**	**91 (42%)**	**85(39%)**
Lost to Follow-up	0 (0%)	0 (0%)	0 (0%)	2 (<1%)	0 (0%)
Pre-Existing Violation	2(<1%)	2 (<1%)	3 (1%)	2 (<1%)	0 (0%)
Protocol Non-Compliance	4 (2%)	5 (2%)	2 (<1%)	2 (<1%)	0 (0%)
Treatment Failure	125 (57%)	92 (40%)	74 (34%)	69 (32%)	69(32%)
Adverse Event	12 (5%)	12 (5%)	16 (7%)	16 (7%)	16 (7%)
Pooled[b]	**(n=452)**	**(n=468)**	**(n=454)[a]**	**(n=435)[a]**	**(n=443)**
Total Completed	**179 (40%)**	**271 (58%)**	**282 (62%)**	**263 (60%)**	**271 (61%)**
Total Withdrawn	**273 (60%)**	**197 (42%)**	**172 (38%)**	**172 (40%)**	**172 (39%)**
Lost to Follow-up	3 (<1%)	1 (<1%)	3 (<1%)	3 (<1%)	1 (<1%)
Pre-Existing Violation	4 (<1%)	3 (<1%)	6 (1%)	4 (<1%)	0 (0%)
Protocol Non-Compliance	14 (3%)	9 (2%)	6 (1%)	9 (2%)	9 (2%)
Treatment Failure	229 (51%)	159(34%)	124 (27%)	128 (29%)	134 (30%)
Adverse Event	23 (5%)	25 (5%)	33 (7%)	28 (6%)	28 (6%)

Derived from Individual Study Reports

a) Total number of patients includes two patients (one in the celecoxib 200 mg BID group [Study 023] and one in the celecoxib 400 mg BID group [Study 022]) who were randomized but did not receive study medication and are not included in the ITT Cohort.

b) Pooled represents data from combined pivotal Studies 022 and 023.

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Table A.44 Time to Withdrawal - Lack of Arthritis Efficacy (023)

[redacted]

TABLE 28
TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
PART 1 OF 2: KAPLAN-MEIER ESTIMATES OF PROPORTION OF PATIENTS WHO DID NOT WITHDRAW DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

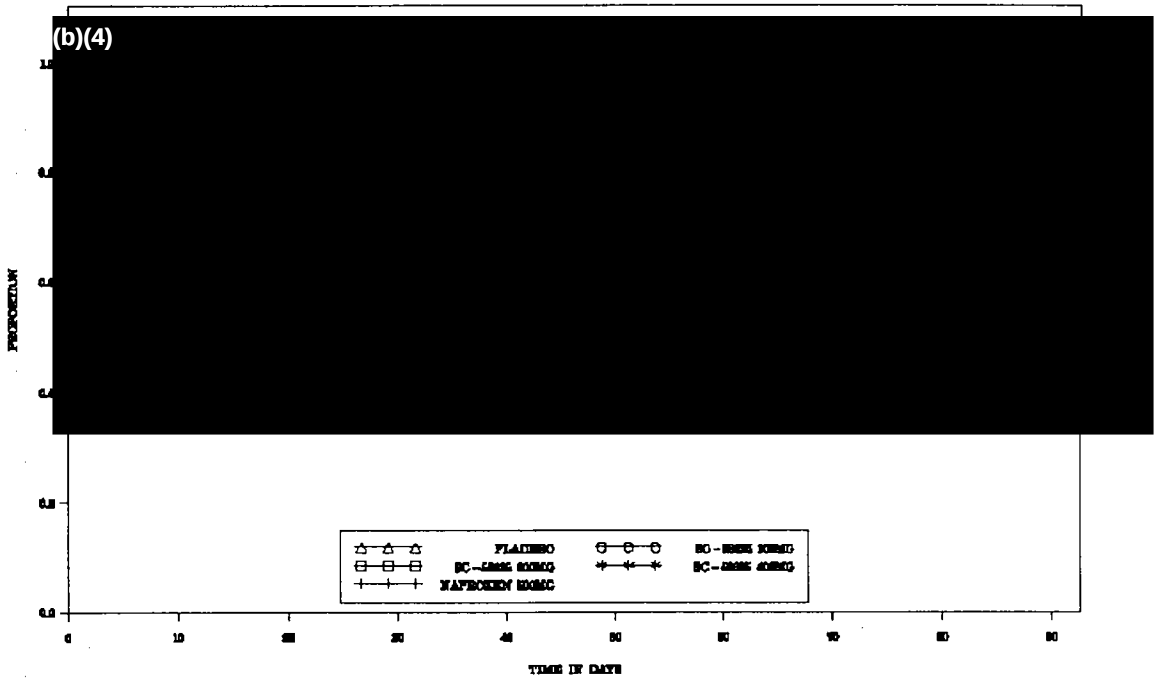


TABLE 28
TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
PART 2 OF 2: LOG-RANK TESTS FOR TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

p-VALUES FOR OVERALL COMPARISONS (a): <0.001

p-VALUES FOR TREATMENT COMPARISONS (b):

100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	NAPROXEN VS. PLACEBO	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
<0.001	<0.001	<0.001	0.092	0.048	0.774	<0.001	0.035	0.647	0.878

(a) From log-rank test for all five treatment groups
(b) From pairwise log-rank test

APPEARS THIS WAY ON ORIGINAL

Table A.45 Summary of Dosage change-OA /RA(protocol 024)

Table 9.7
Summary of Dosage Changes: Long Term Open Label Trial

024 Starting Dose	OA Withdrawals (N = 657)	OA Still Active (N = 1497)	OA Combined (N = 2054)
Celecoxib 100 mg BID			
NO CHANGES	192(29.2%)	604(40.3%)	796(38.9%)
INCREASE IN DOSE	444(67.6%)	1076(71.8%)	1512(73.6%)
100-200	437(66.5%)	1058(70.7%)	1495(72.8%)
100-300	3(0.5%)	1(< 0.1%)	4(0.2%)
100-400	1(0.2%)	0(0.0%)	1(< 0.1%)
OTHER	3(0.5%)	0(0.0%)	3(< 0.1%)
MULTIPLE CHANGES	21(3.2%)	56(3.7%)	77(3.7%)
100 200 100	12(1.8%)	20(1.3%)	32(1.6%)
100-200-100-200	4(0.6%)	18(1.2%)	22(1.1%)
100-200-100-300	3(0.5%)	0(0.0%)	3(< 0.1%)
100-200-100-other-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
100 200 300 200	1(0.2%)	2(0.1%)	3(0.1%)
100-200-300-other-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
100-200-other	1(0.2%)	1(< 0.1%)	2(< 0.1%)
100 200 other 100 200	1(0.2%)	0(0.0%)	1(< 0.1%)
100-300-other-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
100-300-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
100 other 300	1(0.2%)	2(0.1%)	3(0.1%)

"Other" means celecoxib doses of 300 mg AM/200 mg PM, 200 mg AM/100 mg PM, 400 mg AM/300 mg PM, 100 mg QD, or 100 mg TID.

Table 9.7
Summary of Dosage Changes: Long Term Open Label Trial

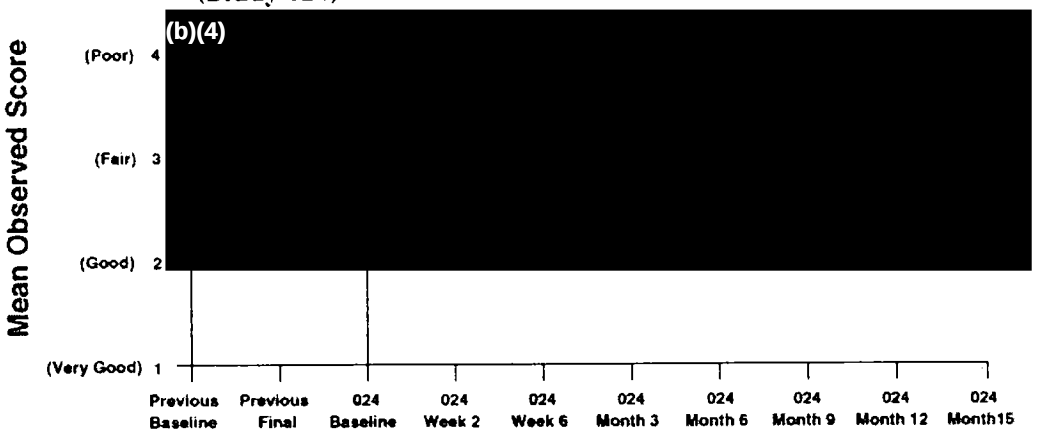
RA Start Dose	RA Withdrawals (N = 523)	RA Still Active (N = 1422)	RA Combined (N = 1945)
Celecoxib 200 mg BID			
NO CHANGES	121(23.1%)	315(22.2%)	436(22.4%)
INCREASE IN DOSE	368(70.4%)	1023(71.9%)	1391(71.5%)
200-300	117(22.4%)	376(26.4%)	493(25.3%)
200-400	251(48.0%)	648(45.6%)	899(46.2%)
OTHER	0(0.0%)	1(< 0.1%)	1(< 0.1%)
DECREASE IN DOSE	4(0.8%)	5(0.4%)	9(0.5%)
MULTIPLE CHANGES	30(5.7%)	79(5.6%)	109(5.6%)
200-100-200	3(0.6%)	4(0.3%)	7(0.4%)
200-100-200-100	1(0.2%)	0(0.0%)	1(< 0.1%)
200-100-200-300	2(0.4%)	1(< 0.1%)	3(0.2%)
200 100 200 300 300	1(0.2%)	0(0.0%)	1(< 0.1%)
200-100-200-300	2(0.4%)	1(< 0.1%)	3(0.2%)
200-100-200-300-200	1(0.2%)	0(0.0%)	1(< 0.1%)
200-100-200-other	1(0.2%)	0(0.0%)	1(< 0.1%)
200 100 300 200	1(0.2%)	0(0.0%)	1(< 0.1%)
200-300-200	1(0.2%)	1(< 0.1%)	2(< 0.1%)
200-300-200-300	1(0.2%)	1(< 0.1%)	2(< 0.1%)
200-300-other	1(0.2%)	1(< 0.1%)	2(< 0.1%)
200 300 other 200	1(0.2%)	1(< 0.1%)	2(< 0.1%)
200-300-other-300	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200-400-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200-400-300	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200-400-other	0(0.0%)	1(< 0.1%)	1(< 0.1%)
200 other 200	1(0.2%)	0(0.0%)	1(< 0.1%)
200 other 300	1(0.2%)	2(0.1%)	3(0.2%)
200 other other	0(0.0%)	1(< 0.1%)	1(< 0.1%)
300-200-300	0(0.0%)	1(< 0.1%)	1(< 0.1%)
300-300-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
300-300-other	0(0.0%)	1(< 0.1%)	1(< 0.1%)
300 other 200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
400-200-300	0(0.0%)	1(< 0.1%)	1(< 0.1%)
400-300-200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
400-300-300	0(0.0%)	1(< 0.1%)	1(< 0.1%)
400-300-other	0(0.0%)	1(< 0.1%)	1(< 0.1%)
400-other-300	0(0.0%)	1(< 0.1%)	1(< 0.1%)
other 200 200	1(0.2%)	0(0.0%)	1(< 0.1%)
other 200 300	0(0.0%)	1(< 0.1%)	1(< 0.1%)
other 300 200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
other 300 300	0(0.0%)	1(< 0.1%)	1(< 0.1%)
other other 200	0(0.0%)	1(< 0.1%)	1(< 0.1%)
other other 300	0(0.0%)	1(< 0.1%)	1(< 0.1%)

"Other" means celecoxib doses of 300 mg AM/200 mg PM, 400 mg AM/200 mg PM, 400 mg AM/300 mg PM, 200 mg QD, or 200 mg TID.

BEST POSSIBLE

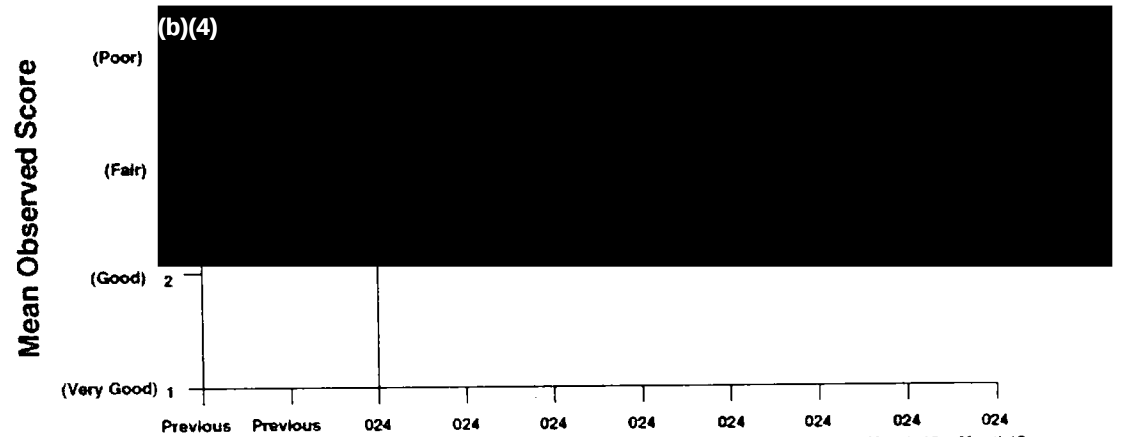
Figure A.1 Patient's Global Assessment-OA/RA (protocol 024)

Figure 7. Patient's Global Assessment of Arthritic Condition: OA Patients (Study 024)



All 2554	2554	2549	2453	2109	1602	990	665	270	84
Celecoxib 1579	1579	1578	1534	1341	1017	629	433	179	67
NSAID 503	502	501	459	349	247	153	89	26	0
Placebo 472	472	470	460	419	338	208	143	65	17

Figure 10. Patient's Global Assessment of Arthritic Condition: RA Patients (Study 024)



All 1945	1945	1943	1865	1669	1439	1089	722	294	111
Celecoxib 1197	1197	1197	1155	1039	890	672	455	193	78
NSAID 360	360	360	331	280	235	163	99	18	0
Placebo 388	388	386	379	350	314	254	168	83	33